REMARKS/ARGUMENTS

With this amendment, claims 6-34 are pending. Claims 1-5 and 35-55 are withdrawn. For convenience, the Examiner's rejections are addressed in the order presented in the March 22, 2006 Office Action.

I. Status of the claims

Claims 6 and 21 are amended to recite "propagating pancreatic cells that exhibit a CD56 protein as a cell surface marker". Support for these amendments is found throughout the specification, for example at page 6, lines 22-32. These amendments add no new matter and are not limiting amendments.

II. Rejections under 35 U.S.C. §112, second paragraph

Claims 6-34 are rejected for allegedly being indefinite. According to the Office Action the claims do not clearly state which cell population is used to create a propagating pancreatic cell line. In order to expedite prosecution, claims 6 and 21 are amended to recite "propagating pancreatic cells that exhibit a CD56 protein as a cell surface marker". In view of this amendment, withdrawal of the rejection for alleged indefiniteness is respectfully requested.

III. Rejections under 35 U.S.C. §103(a)

Claims 6-34 are rejected as allegedly obvious over Fung *et al.*, (US Patent No. 6,326,201) and Shipley *et al.* The claims are directed to a method of obtaining a culture of propagating pancreatic cells that express a CD56 protein as a cell surface marker. Method steps include isolating pancreatic cells from a pancreas; contacting the pancreatic cells with a CD56 binding reagent; selecting pancreatic cells that specifically bind to the CD56 binding reagent; and separating them from pancreatic cells that do not bind the CD56 binding reagent. To the extent the rejection applies to the amended claims, Applicants respectfully traverse the rejection.

The Office Action has not established a case of *prima facie* obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be

some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference must teach or suggest all the claims limitations. MPEP§2143. See also *In re Rouffet,* 47 USPQ2d 1453. The court in *Rouffet* stated that "even when the level of skill in the art is high, the Board must identify specifically the principle, known to one of ordinary skill, that suggests the claimed combination." *Rouffet* at 1459. The court has also stated that actual evidence of a suggestion, or teaching, or motivation to combine is required and the showing of a suggestion, or teaching, or motivation to combine must be "clear and particular." *In re Dembiczak*, 50 USPQ2d 1614, 1617 (1999). The cited references do not meet this standard.

According to the Office Action, Fung *et al.* teaches a method to obtain propagating pancreatic cells, including isolation with labeled antibodies. The Office Action also alleges that Shipley *et al.* teaches that CD56 is expressed in pancreatic islets and that the marker can be used to isolate pancreatic cells. *See, e.g.*, Office Action at page 4. At page 5, the Office Action alleges that the combination of Shipley *et al.* and Fung *et al.* would have been obvious to one of skill and that Shipley *et al.* would provide a reasonable expectation of success and therefore motivate those of skill to use CD56 as a labeled binding reagent in the methods of Fung *et al.* Applicants respectfully disagree.

First, Applicants dispute the alleged teachings of the cited references. Fung *et al.* teach a method of isolating propagating pancreatic cells that relies on a first step of dissecting pancreatic ducts from a pancreas. The use of antibodies to isolate cells from this population is disclosed only generally by the reference and the Office Action agrees that Fung *et al.* does not provide any teaching of specific CD56 antibodies or other CD56-binding reagents to isolate pancreatic cells that express CD56. *See, e.g.*, Office Action at page 4.

Shipley *et al.* does not teach or disclose methods to isolate propagating pancreatic cells that express CD56. Shipley *et al.* teach only detection of the CD56 protein in fixed, embedded tissue samples, not CD56 antibody-based isolation of living cells that can be propagated. Shipley *et al.* were able to detect CD56 protein with a CD56 antibody only after performing a harsh epitope retrieval protocol. The samples were incubated in an alkaline

solution (pH 6.0) and then microwaved on high for two ten minute periods before incubation with the CD56 antibody. *See, e.g.*, Shipley *et al.* at page 88, left column. With regard to the type of cells detected by the CD56 antibody, Shipley *et al.* disclose only that pancreatic islet cells were weakly stained with the CD56 antibody. *See, e.g.*, Shipley *et al.* at page 88, Table 1; page 90, left column; and page 92, left column.

One of skill in the art would not have been motivated to use a CD56 antibody in the methods allegedly disclosed by Fung *et al.* based on the disclosure of Shipley *et al.* Moreover, the combination of the two references would render the method of Fung *et al.* inoperative. The end product of Fung *et al.* is allegedly a culture of living and proliferating pancreatic progenitor cells. Shipley *et al.* teaches that pancreatic cells must be incubated in an alkaline solution and then microwaved at highest power for two ten minute intervals in order to present a CD56 epitope that can be detected by CD56 antibodies. A living pancreatic cell would not survive this treatment and thus, those of skill would not be motivated to combine the methods of Fung *et al.* and Shipley *et al.* Fung *et al.* describe their product progenitor cells as "an undifferentiated cell which is capable of differentiation . . ." and whose progeny differentiate. In contrast, Shipley *et al.* disclose that CD56 antibodies detect pancreatic islet cells. See, *e.g.*, Fung *et al.* at column 12, lines 36-50. Pancreatic islet cells are mature, terminally-differentiated cells that secrete hormones, *e.g.*, insulin, somatostatin, and glucagon, but that do not continue to differentiate or divide. Thus, Shipley *et al.* teach only that CD56 antibodies are useful to identify non-dividing, differentiated pancreatic cells. Based on these disclosures by Shipley *et al.*, one of skill would not be motivated to use a CD56 antibody in the methods of Fung *et al.* to obtain a population of living and proliferating pancreatic progenitor cells.

In view of the above arguments and remarks, withdrawal of the rejection under 35 U.S. C. §103(a) is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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